Harvesting syncytial nuclear aggregates for prenatal genetic diagnostics

A combination of antibodies to be used to separate syncytial nuclear aggregates from maternal blood.

The technology is a combination of several antibodies reactive with proteins on the surface of syncytial nuclear aggregates. Syncytial nuclear aggregates are large fragments of the surface layer of the placenta, that are shed into the maternal blood in all pregnancies. Since they are multinucleated fragments of placental origin, syncytial nuclear aggregates contain multiple fetal nuclei. The antibodies will enable isolation of individual syncytial nuclear aggregates from a maternal blood sample. The individual syncytial nuclear aggregates will then be subjected to karyotype analysis to detect fetal genetic abnormalities or confirm the fetus is genetically normal.

These antibodies are coupled to commercially available magnetic beads which are incubated with a maternal blood sample. Syncytial nuclear aggregates are targeted by the antibodies and become attached to the magnetic beads which we then collect using a magnet. The syncytial nuclear aggregates are then identified using a fluorescently-tagged monoclonal antibody developed by us which is reactive with an intracellular antigen. This helps us to physically identify the syncytial nuclear aggregates which remain in a large pool of magnetic beads with some other contaminating cells and also aids in confirming the fetal nature of the syncytial nuclear aggregates.

We have demonstrated that syncytial nuclear aggregates that we produce from human placentae in vitro, are suitable for genetic diagnosis. We have demonstrated that we can amplify the genetic material in a single syncytial nuclear aggregate which is of suitable quality to conduct genetic analysis by the method of array comparative genome hybridisation. Using this technique we have shown that multiple syncytial nuclear aggregates from the sample placenta produce the same karyotype.

Application

Antibodies to separate syncytial nuclear aggregates to be used in development of a kit to detect prenatal genetic abnormalities.

Key Aspects

- Syncytial nuclear aggregates (SNA’s) can be used to detect all known genetic abnormalities, which is a significant advantage over current cell-free fetal DNA, which can only detect limited number of genetic abnormalities.
- The antibodies can be applied to existing diagnostic technologies and will also be able to use diagnostic technologies that are currently under development.
The Department of Obstetrics and Gynaecology, at The University of Auckland, New Zealand

Associate Professor Larry Chamley is a reproductive immunologist and placentologist. He is the author of more than 100 peer-reviewed publications and has had previous success in commercialising antibodies. Professor Chamley’s expertise in this field is recognised internationally by his membership of the Editorial Boards of the journals Placenta - Trophoblast Research, the American Journal of Reproductive Immunology and the Journal of Reproductive Immunology, as well as his election to the Executive Councils of several societies including the Society for Reproductive Biology, The Australia and New Zealand Placental Research Association and the International Federation of Placenta Associations. He has a number of research projects currently underway examining the physiological role of shed trophoblasts in pregnancy, with funding from a variety of sources including the Marsden Fund and the Auckland Medical Research Foundation.

Professor Stone is Professor of Maternal Fetal Medicine at The University of Auckland and Consultant Obstetrician at Auckland City Hospital. He has a long-standing interest in the diagnosis of fetal abnormalities and has been instrumental in the implementation of the education about the Nuchal Translucency screening technique in the Auckland region. Professor Stone was a member of the New Zealand Antenatal Advisory Group for the National Screening Unit of the Ministry of Health. This group has reviewed the international literature on the subject and has made recommendations to the Minister of Health on the most efficacious screening methods for New Zealand. Professor Stone has established on-going links with the national Down’s syndrome screening programmes in the UK (Professor Nick Wald, Wolfson Institute of Preventive Medicine, London UK) and in Ontario, Canada.

IP Position
Both the antibodies and combination of antibodies is novel. We are seeking to partner the antibodies with a company that has developed or is developing a prenatal genetic diagnostic.

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